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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/883,550	06/18/2001	William E. Marshall	P01936US5	1897

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SUITE 3200
DES MOINES, IA 50309-2721

EXAMINER	
ZEMAN, ROBERT A	
ART UNIT	**PAPER NUMBER**
1645	

MAIL DATE	DELIVERY MODE
07/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/883,550	MARSHALL, WILLIAM E.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-8,10-12 and 14-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-8,10-12 and 14-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Appeal Brief filed on 9-25-2006 is acknowledged. In light of a careful review of the record, the finality of the previous Office action is withdrawn. Claims 1.4-8, 10-12 and 14-19 are pending and currently under examination.

Claim Rejections Withdrawn

The rejection of claims 1, 4-8, 10-11, 14-15 and 17-19 under 35 U.S.C. 103(a) as being unpatentable over De Vuyst et al. (Microbiology, Vol. 142, 1996, pages 817-827) is withdrawn.

The rejection of claims 1, 4-8, 10-15 and 17-19 under 35 U.S.C. 103(a) as being unpatentable over De Vuyst et al., cited above, in view of Nanji (U.S. Patent 5,413,785 – IDS-2) is withdrawn.

The rejection of claim 16 under 35 U.S.C. 103(a) as being unpatentable over De Vuyst et al., cited above, in view of Perdigon et al. (Journal of Food Protection Vol. 53, No. 5, pages 404-410, 1996 – IDS-2) is withdrawn.

New Claim Objections

Claim6 and 7 are objected to because of the following informalities: claim 6 is objected to since genus names should be italicized. Claim 7 is objected to since abbreviations should be spelled out upon their first recitation. Appropriate correction is required.

New Grounds of Rejection

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-6, 8, 10-12 and 14-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for modulating the immune system of an animal comprising exposing bacterial to two or more sequential periods of stress; separating said bacteria from the medium; filtering clarified medium to remove all substances with a molecular weight greater than 10kDa; and administering the filtrate to said animal wherein the bacteria is *L. caseii, L. acidophilus, L. fermentum, L. plantarum, L. monocytogenes, S. aureus, S. typhimurium, P. acidolactici, B. coryneforme, E. coli, E. faecium, S. pyogenes or K. pneumoniae*, does not reasonably provide enablement for said method of modulating the immune system of an animal utilizing any other species of bacteria. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The practice of this invention requires the use of bacteria that release certain low molecular weight stress release factors (SRFs) after exposure to sequential periods of stress and wherein said SRFs are capable of modulating the immune system of the an animal when administered to said animal.

Breadth of the claims: The claims are extremely broad as they encompass **all** bacterial species.

Guidance of the specification/The existence of working examples: To use the instant invention the skilled artisan must know which bacterial species are capable of producing SRFs

(in response to the recited stresses) that are capable of modulating the immune system upon its administration to an animal. The specification discloses that only 13 different species of animal-associated bacteria were found to "release products when stressed" (see page 4). The specification further discloses that the distribution of polymer:oligomer:monomer is not equal among the species (see page 4). Finally, the only bacterial species that were shown to release A254 absorbing compounds were set forth in Table 1 (see Example 1 on pages 16-17). Finally, of those bacterial strains set forth in Table 1 only *L. caseii* was shown to activate monocytes and the *Lactobacillus* species were demonstrated to increase monocyte survival.

State of the art: At the time of applicants' invention the art of using products produced by stressed bacteria (with a molecular weight less than 10 kDa) to modulate the immune system of an animal was underdeveloped. While the use of heat shock proteins has been known in the art for years, the use of low molecular weight products is limited (see De Vuyst et al. (Microbiology, Vol. 142, 1996, pages 817-827, of record).

Predictability of the art and the amount of experimentation necessary: People of skill in the art require evidence that a benefit can be derived by the therapeutic application of a given substance; however, a survey of the relevant art does not indicate that substances such as those claimed provide such benefit. The instant specification fails to provide significant direction on which bacteria, other than those set forth in Table 1, are capable of eliciting a modulated immune response when administered to an animal. Moreover, the specification is silent as to which "product" within the <10kDa fraction is responsible for said modulation. Finally, as the response of individual species of bacteria to various stressors is quite variable, and the "identity" of the immunomodulatory unknown, the efficacy of a given <10kDa fraction from a given stressed

bacteria has to be determined empirically. Given the enormous number bacterial species encompassed by the claims and the lack of guidance regarding the identity of the immunomodulatory, this constitutes undue experimentation.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

ROBERT A. ZEMAN
PRIMARY EXAMINER
July 3, 2007